

## REMARKS

Applicants provide preliminary comments directed to an issue that appears to be central to all of the rejections set forth in the Final Office Action. The Final Office Action challenges the sufficiency of the previously presented Declaration under 37 C.F.R. 1.132 of Dr. Ulrike Wachendorff-Neumann. See Final Office Action at pages 2-3, as well as page 8 (top) with respect to an obviousness-type double patenting rejection and at pages 13 (bottom) and 15 (middle) with respect to the obviousness rejection. More specifically, the Final Office Action at page 2 states that “the Declaration identifies different compounds {i.e., Example 2, Example 4, Example 6, etc.} of the instant claimed invention which are being compared but in each case {Table I (page 3), Table II (page 5), Table II (page 7) and Table IV (page 9)}, the same structure is displayed” (emphasis added). Applicants emphasize that the Declaration does not identify “different compounds” in the even-numbered examples of the Declaration.

First, the Example numbers used in the Declaration are clearly nothing more than a sequential listing that pertains only to the Declaration. No representation was made that the example numbers used in the Declaration were intended to correlate with any numbers for examples of the specification (or the reference). Quite to the contrary, each Table of the Declaration clearly shows that the odd-numbered examples refer to known compounds described in specific examples of the cited references. That is, Table I specifically indicates that Example 1 of the Declaration was carried out using the compound of Example 4.32 of WO 2002/059086, and Tables II, III, and IV specifically indicate that Examples 3, 5, and 7 of the Declaration were carried out using the compound of Example 21 of CA 2474902. In short, the odd numbers used in the Declaration for the comparison examples do not correspond to or correlate with Examples 1, 3, 5, and 7 of Applicants’ specification.

Similarly, the even numbers used in the Declaration do not correspond to or correlate with Examples 2, 4, 6, and 8 of the specification. The reason the same structure is displayed in each of the tables of the Declaration is that a single compound was used in each such example. Although not identified by number in the Declaration, this compound is disclosed as Applicants’ Ex. 9 (shown in Table 1 at pages 40-41 of the specification). Applicants do apologize for any confusion the absence of an identifying number from the specification may have caused but point

out that the formula shown in the Declaration clearly and fully describes a specific compound described in their specification and included within their claims.

Applicants thus submit that the Declaration of Dr. Wachendorff-Neumann shows what it purports to show – that (1) an inventive compound having a difluoromethyl substituent on the thiazole moiety is superior to a known comparison compound having a trifluoromethyl substituent and (2) an inventive compound having an N-substituted bridging amide nitrogen atom is superior to a known comparative unsubstituted compound.

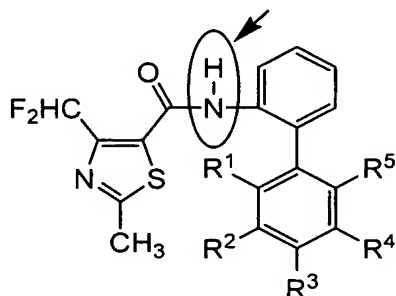
#### Allowable Subject Matter

Applicants again gratefully acknowledge the indication in the Final Office Action that Claims 26 and 28 stand objected to as being dependent upon a rejected base Claim 18. However, in view of the previously presented amendments and data presented in the Declaration of Dr. Wachendorff-Neumann, Applicants have again not amended Claims 26 and 28 as kindly suggested by the Examiner but instead submit that all pending claims are allowable as written.

#### Double Patenting Rejection

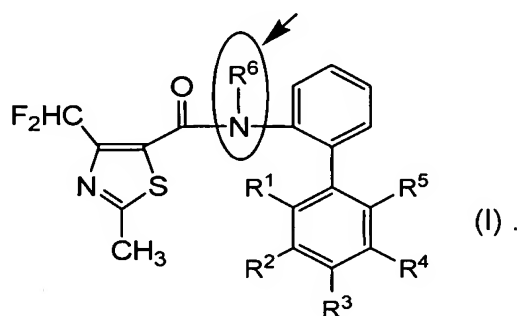
Claims 18-25, 29, and 31-33 stand provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Claims 22-33 and 35-37 of copending Application No. 10/502,994. Applicants again respectfully traverse.

As discussed in Applicants' previous Amendment, the '994 application is directed to carboxamides of the formula



in which R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, and R<sup>5</sup> are independently hydrogen, halogen, cyano, nitro, (halo)alkyl, alkenyl, (halo)alkoxy, (halo)alkylthio, (halo)alkylsulfonyl, or cycloalkyl, or R<sup>1</sup> and R<sup>2</sup> together or R<sup>2</sup> and R<sup>3</sup> together can be optionally substituted alkylene. E.g., page 1, lines 11-24. It is clear on its face that the '994 application discloses only an

unsubstituted amide group (as shown by the oval and arrow above), whereas Applicants' claims are directed to compounds in which the bridging amide group must be N-substituted as shown below in formula (I) by the oval and arrow



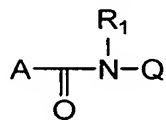
Notwithstanding the clear teaching of the '994 application, the Final Office Action at page 4 asserts that such substitution would be obvious. Even if (solely for the sake of discussion) a prima facie case of obviousness has been established – a position not conceded by Applicants for reasons similar to those presented in their previous Amendment – Applicants maintain that Dr. Wachendorff-Neumann's Declaration shows that a representative compound of their invention in which the bridging amide nitrogen atom is N-substituted exhibits unexpectedly enhanced activity when compared to a corresponding unsubstituted compound within the teachings of the '994 application.

Applicants therefore respectfully maintain that their claimed invention is patentably distinct from the '994 application and thus do not at this time offer a terminal disclaimer.

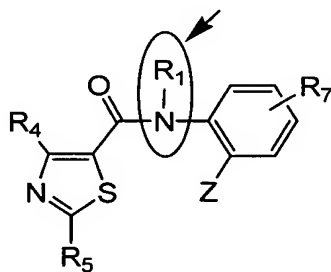
#### Rejection under 35 U.S.C. 103

Claims 18-25, 27, and 29-33 stand rejected under 35 U.S.C. 103(a) as being unpatentable over WO 02/059086 ("Walter et al") and CA 2,474,902 ("Elbe et al"), each taken alone or in combination with each other and each in further combination with JP 08/176112 ("Kanji et al"). Applicants again point out that Elbe et al is a Canadian counterpart of the '994 application (discussed above with respect to double patenting) and that that Walter et al is a counterpart of published US 2004/0138265. Applicants again respectfully traverse.

As fully discussed in Applicants' previous Amendment, **Walter et al** discloses microbicidal carboxamides having the general formula

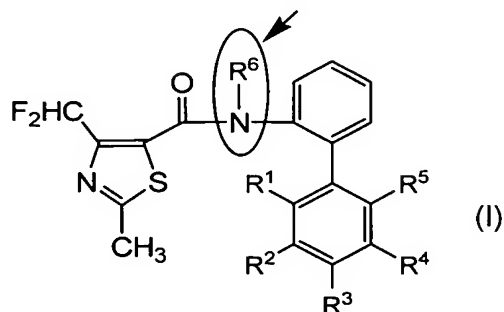


in which A represents any of several heterocycles, Q represents any of several aromatic groups, and R<sub>1</sub> represents an unsaturated hydrocarbon group having at least one carbon-carbon multiple bond or a carbonyl group. E.g., pages 1-2. Included within this large array of possibilities are compounds in which A is group (A3) and Q is group (Q1) represented by the following formula:



wherein R<sub>1</sub> is CH-C≡C-R<sub>2</sub>, CH<sub>2</sub>CH=CHR<sub>2</sub>, CH=C=CHR<sub>2</sub>, or COR<sub>3</sub>; R<sub>2</sub> is hydrogen or one of several carbon-containing substituents; R<sub>3</sub> is optionally substituted C<sub>1</sub>-C<sub>6</sub>alkyl (in which the optional substituent is halogen, C<sub>1</sub>-C<sub>6</sub>alkoxy, or C<sub>1</sub>-C<sub>6</sub>haloalkoxy) or is C<sub>1</sub>-C<sub>6</sub>alkylthio, C<sub>1</sub>-C<sub>6</sub>haloalkylthio, C<sub>1</sub>-C<sub>6</sub>alkoxy, C<sub>1</sub>-C<sub>6</sub>haloalkoxy, C<sub>3</sub>-C<sub>6</sub>alkenyloxy, C<sub>3</sub>-C<sub>6</sub>haloalkenyloxy, C<sub>3</sub>-C<sub>6</sub>alkynyloxy, or C<sub>3</sub>-C<sub>6</sub>haloalkynyloxy; R<sub>4</sub> is methyl that is optionally fluorinated (including, among others, CF<sub>2</sub>H) or is chlorine or bromine; R<sub>5</sub> is methyl or one of three other narrowly defined groups; and Z is phenyl or halophenyl, optionally substituted C<sub>5</sub>-C<sub>7</sub> cycloalkyl, or a branched alkyl group. E.g., page 1, second paragraph, continuing over to page 2. That is, Walter et al discloses compounds in which, inter alia, the bridging amide group (shown by the oval and arrow above) is substituted with either an unsaturated hydrocarbon group having at least one carbon-carbon multiple bond or a carbonyl group connected to a narrowly defined set of optionally substituted alkyl, alkoxy, alkylthio, alkenyloxy, or alkynyloxy groups (i.e., COR<sub>3</sub>).

In contrast, Applicants' claims are directed to thiazolylbiphenylamides of formula (I)



in which the bridging amide nitrogen atom (again shown by the oval and arrow above) is substituted by either (1) non-carbonyl  $R^6$  groups that are entirely different from the unsaturated hydrocarbon groups taught by Walter et al or (2) certain carbonyl-containing  $R^6$  groups.

First, Applicants maintain that the compounds of their invention in which the amide substituent is not a carbonyl group are not taught or suggested by Walter et al, even without reference to Dr. Wachendorff-Neumann's Declaration, and thus maintain that those skilled in the art would not be led by Walter et al to such compounds. Applicants' Claim 29 is one example of a claim directed to such nonobvious subject matter.

Second, Applicants maintain that compounds of their invention in which the amide substituent is attached to a carbonyl group are also patentably nonobvious over Walter et al. Applicants again acknowledge that their group  $R^6$  can include carbonyl groups similar to the carbonyl group  $COR_3$  of the reference. In particular, among the many meanings of  $R_1$  of the reference can be found a carbonyl group  $COR_3$  in which  $R_3$  is an optionally substituted alkyl group or an alkoxy or haloalkoxy group. At first glance, this might seem suggestive of compounds of Applicants' invention in which  $R^6$  represents  $-COR^7$  in which  $R^7$  is an alkyl, alkoxy, alkoxyalkyl, haloalkyl, haloalkoxy, or haloalkoxyalkyl group. However, this aspect of Walter et al must be viewed in proper context. To arrive at compounds of this type, one would need to select only one of the five heterocyclic structures of group A (i.e., specifically thiazoles (A3)), no more than two of the ring structures of group Q (i.e., specifically substituted phenyl group (Q1) and perhaps group (Q6)), only one of the several groups specified for group  $R_4$  (i.e., specifically  $CF_2H$ ), and only one of the several

groups specified for group  $R_1$  (i.e.,  $COR_3$ , and even then only for some of the substituents  $R_3$ ). However, Walter et al does not describe the particular combination of structural features that characterize the carbonyl-containing embodiments of Applicants' claimed invention and does not show even one specific example of a compound in which A is a thiazole and  $R_4$  is a group other than  $CF_3$ . See list at page 11, as well as entries 4.01 through 4.46 in the table at pages 31-33. Applicants in this respect (i.e., for embodiments in which  $R^6$  is a carbonyl group) again refer to the Declaration of Dr. Wachendorff-Neumann for its showing that the difluoromethyl substituent of the thiazole moiety provides significantly greater activity than a trifluoromethyl substituent as disclosed in Walter et al (as shown in Ex. 4.32 at page 33 of the reference).

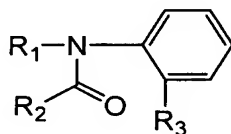
Applicants therefore maintain that their claimed invention is not rendered obvious by Walter et al taken alone.

As discussed above with respect to the obviousness-type double patenting rejection, **Elbe et al** discloses carboxamides in which the bridging amide nitrogen atom is not N-substituted, whereas the compounds of Applicants' invention must be N-substituted. For essentially the reasons as discussed above with respect to the double-patenting rejection, Applicants submit that Elbe et al would not itself lead those skilled in the art to their claimed invention. Applicants further submit that Elbe et al, even when taken with Walter et al, would not lead those skilled in the art any closer to their claimed invention than what is already disclosed in Walters et al.

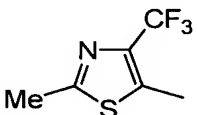
As pointed out in Applicants' previous Amendment and as further discussed above with respect to the counterpart '994 application, Dr. Wachendorff-Neumann's Declaration shows that an inventive N-substituted thiazole compound exhibits enhanced activity compared to the corresponding compound of Elbe et al in which the amide nitrogen atom is not substituted (see Ex. 21 of Elbe et al).

Applicants therefore submit that their claimed invention is patentably distinct from Elbe et al, whether taken alone or with Walter et al.

Applicants maintain that Kanji et al would not lead those skilled in the art to their claimed invention. **Kanji et al** discloses carboxamides of the formula



in which  $R_1$  can be any number of groups, including acyl groups of formulas  $-CO-R_4$  (where  $R_4$  can be alkyl, haloalkyl, or phenoxyethyl) or a second amide moiety  $-CO-NH-R_5$  (where  $R_5$  can be alkyl or phenyl), as well as certain ethers  $R_6$  or alkyl groups  $R_7$ ;  $R_2$  can be a variety of cyclic groups, including a specific trifluoromethyl-


substituted thiazole moiety having the formula ; and  $R_3$  can be any of

a variety of cyclic or unsaturated groups, including phenyl. E.g., pages 1-2 (as well as *Patent Abstracts of Japan*). Kanji et al, however, does not teach or suggest thiazoles having any other substitution pattern and does not teach or suggest a difluoromethyl substituent such as required by Applicants. Moreover, Kanji et al does not disclose compounds in which the amide nitrogen atom is substituted with a formyl group (i.e., where  $R_4$  of the reference could be hydrogen) or any other acyl groups specified by Applicants. Applicants note with respect to the second amide moiety  $-CO-NH-R_5$  taught by Kanji et al that this second amide group must always have one hydrogen atom and one alkyl or phenyl substituent. For embodiments of Applicants' claimed compounds in which  $R^6$  can be a second amide substituent  $-CONR^8R^9$ , neither  $R^8$  nor  $R^9$  can be hydrogen. Therefore, even if Kanji et al could be read to suggest the interchangeability of the groups it discloses as asserted in the Final Office Action, Applicants submit that Kanji et al would not lead those skilled in the art to the particular embodiments they claim. Finally, as already discussed above, Dr. Wachendorff-Neumann's Declaration shows the significance of difluoromethyl substitution instead of trifluoromethyl substitution in the thiazole moiety and thus further supports Applicants' position that their claimed invention is patentably distinct from anything taught or suggested by Kanji et al.

Applicants therefore respectfully submit that their claimed invention is not rendered obvious by Walter et al and Elbe et al, whether taken alone or in combination with each other or in further combination with Kanji et al.

In view of the preceding amendments and remarks, allowance of the claims is respectfully requested.

Respectfully submitted,

By   
Richard E. L. Henderson  
Attorney for Applicants  
Reg. No. 31,619

Bayer CropScience LP  
2 T.W. Alexander Drive  
Research Triangle Park, NC 27709  
Ph.: (919) 549-2183  
Fax: (919) 549-3994

q:patents/prosecution documents/cs8479/cs8479 amendment